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Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

RECEIVED
4/3/95

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment. See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).

o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.

othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See*, 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

[6] 43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112

"Birth Defects" listed.

[14] Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

CAS # 105-65-7
Chem: Diisopropyl xanthogen disulfide
Title: Acute oral test; Repeated Oral test; Primary Irritationa nd skin sensitization
Date: 10/4/63
Summary of Effects: Clinical and pathological evidence of cumulative toxicity

Haskell Archives File

Copies to: P. R. Johnson (6)

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 113-63 MR NOS. 526, 10 -/

Material Tested: Diisopropyl Xanthogen Disulfide — Haskell No.: 2766

Submitted by: R. G. Arnold, Elastomer Chemicals Department, Research Division — Other Codes: LRI-142

ACUTE ORAL TEST

Procedure: The test material was administered by stomach tube as a solution in acetone:peanut oil (1:10) in single doses to young adult ChR-CD male rats. Survivors were sacrificed 9-11 days later.

Results:

Sol'n %	Dose (mg/kg)	Mortality*	Toxic Signs	Pathologic Changes	ALD
10	3400	D - 1 d.	Lethal Doses: Weight loss, discomfort, weakness, pallor, irregular respiration, salivation, diarrhea, cyanosis, excessive water intake and urination	Lethal Doses: Dehydration, liver injury; hemorrhagic gastritis at 3400 mg/kg, albumin in kidney at 2250 and 1500 mg/kg	1500 mg/kg
10	2250	D - 1 d.			
10	1500	D - 2 d.			
10	1000	S - 9 d.			
10	670	S - 10 d.	Nonlethal Doses: Weight loss for 2 days at 450 mg/kg and above, initial weight loss at 300 and 200 mg/kg, discomfort, irritability, pallor, diarrhea, excessive water intake and urination at 450 mg/kg and above for 2 days	Nonlethal Doses: None attributable to test compound	
10	450	S - 9 d.			
2	300	S - 11 d.			
2	200	S - 11 d.			

REPEATED ORAL TEST

Procedure: The test material was administered daily by stomach tube as a 10% solution in acetone:peanut oil (1:10) to each of six ChR-CD male rats, 5 times a week for 2 weeks. Groups of 3 animals, along with controls, were killed 5 hours and 10 days after the last treatment.

* D - ( ) d. = Found dead ( ) days after dosing.
S - ( ) d. = Sacrificed ( ) days after dosing.

Results:

Dose (mg/kg/day)	Mortality	Toxic Signs	Pathologic Changes
300	0/6	First week: Severe weight loss for 3 days, excessive urination, discomfort, irritability, pallor and cyanosis. Second week: Weight gain inferior to controls, other signs same but less severe. Observation period: Weight gain parallel to controls, no toxic signs	After 10th treatment: Albumin in kidney, depression of spermatogenesis. After 10-day observation period: None attributable to compound.

PRIMARY IRRITATION AND SKIN SENSITIZATION TESTS

Procedure: In the test for irritation, one drop of a solution of the test material in 1:1 acetone-dioxane containing 13% guinea pig fat (f.a.d.) was applied to the intact shaved skin of 10 male albino guinea pigs. In the test for sensitization, nine applications to abraded skin were made during a 3-week period with 0.05, 0.1, 0.2 and 0.5% solutions in f.a.d. (1,1,2 and 6 applications, respectively). Following a two-week rest period, a challenge test was done which consisted of applying a 0.5% and 0.2% f.a.d. solution of the test material to intact and abraded skin, respectively. In addition, another group of 10 male guinea pigs was tested for skin sensitization by giving each of them an intradermal injection of 0.1 ml of a 0.5% solution of the test material in propylene glycol in the sacral region; these animals were given challenge tests two and three weeks later by applying a 0.5% and 0.2% f.a.d. solution of the test material to intact and abraded skin, respectively.

Results:

Concentration %	24-Hour Irritation		Sensitization	
	Intact Skin	Abraded Skin	Scratch Method*	Intradermal Method**
5.0	Strong	-	9/10	7/10
0.5	None	-		
0.2	-	None		

* By both intact and abraded skin. ** By intact skin only.

Comments: Diisopropyl xanthogen disulfide is moderately toxic when administered to rats in single doses, its Approximate Lethal Dose (ALD) being 1500 mg/kg of body weight. The compound also produced clinical and pathologic evidence of cumulative toxicity; it appeared to injure the stomach and liver, and affect the kidney.

Diisopropyl xanthogen disulfide is a very strong skin irritant and a very potent skin sensitizer.

The compound should be handled with care; skin contact should be avoided.

Report by: Henry Sherman

Approved by: John A. Zapp

HS/mfs
Date: October 4, 1963

Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP (CAP)

Submission number: 12218 A

TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) (SBTOX) (SEN) w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

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entire document: (0) 1 2 **pages** 1, 1st tab **pages** 1, all tabs.

Notes:

Contractor reviewer : LPS **Date:** 5/17/95

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA/ Submission # RFHQ: 1092-12218 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: E.I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(REFER) REFER TO CHEMICAL SCREENING
(CAP) CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/ONGOING
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CERAD DATE: 04/03/95

CHEMICAL NAME:

CAS#: 105-65-7

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
(0213)	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECOTOX/AQUA TOX	01 02 04
0221	ENV. OCCURREL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQUEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
(0228)	ALLERG (ANIMAL)	01 02 04
0229	METAB/PHARMACO (ANIMAL)	01 02 04
0230	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0301	IMMUNO (ANIMAL)	01 02 04
0302	IMMUNO (HUMAN)	01 02 04
0303	CHEM/PHYS PROP	01 02 04
0304	CLASTO (IN VITRO)	01 02 04
0305	CLASTO (ANIMAL)	01 02 04
0306	CLASTO (HUMAN)	01 02 04
0307	DNA DAMG/REPAIR	01 02 04
0308	PROD/USE/PROC	01 02 04
0501	MIDS	01 02 04
0599	OTHER	01 02 04

TRIAGE ENTRY: CAS SR

NON-CBI INVENTORY: (YES) NO

ONGOING REVIEW: YES (DROP/REFER) NO (CONTINUE)

SPECIES: RAT GP

TOXICOLOGICAL CONCERN:
(LOW) Dermal Irritation (0.5%), Acute Oral Toxicity, Subacute Oral Toxicity
(MED) Dermal Sensitization, Dermal Irritation (5.0%)
HIGH

USE:

PRODUCTION:

#12218A
M

Dermal sensitization is of medium concern based on skin responses in 9/10 guinea pigs utilizing the scratch method, and in 7/10 guinea pigs utilizing the intradermal method.

M

Dermal irritation is of medium concern based on strong irritation in guinea pigs exposed to 5.0% concentration.

L

Dermal irritation is of low concern based on no irritation in guinea pigs exposed to 0.5% concentration.

L

Acute oral toxicity is of low concern based on an approximate lethal dose of 1500 mg/kg in rats. Mortality and corresponding doses (mg/kg) were 0/1 (200, 300, 450, 670, 1000), and 1/1 (1500, 2250, 3400). Clinical signs included weakness, breathing irregularities, and cyanosis in the decedents, and irritability at 450 and 670 mg/kg. Pathological changes included liver injury, hemorrhagic gastritis (3400) and albumin in the kidneys (1500, 2250).

L

Subacute oral toxicity is of low concern based on 0/6 deaths in rats exposed to 300 mg/kg, 5 times/week for 2 weeks. Irritability, cyanosis, weight loss, albumin in kidney and depression of spermatogenesis were observed during treatment protocol.